818

PREDICTIVE VALUE OF DNA CONTENT IN HEAD AND NECK CARCINOMA (HNC) TREATED WITH HYPERFRATIONATED RADIOTHERAPY (HRT)

E.Martínez, F.Arias, MA.Domínguez, JJ.Illarramendi, R.López, M.Tejedor, B.Larrínaga*, E.Almudevar**, A.Rubio, P.Soto, JJ.Valerdi. Services of Oncology and Pathology, Hospital de Navarra, Pamplona. SPAIN.

We have studied retrospectively DNA content in biopsy samples of 22 HNC tumors treated by HRT.
From July/89 to October/91, 22 patients (pts) with squamous HNC carcinoma were treated with HRT (two fractions of 1.6 Gy/day, total dose of 64 Gy) and concurrent cisplatin (20 mg/sqm days 1 to 5). Distribution by anatomic site were: oropharynx 8; larynx 7; oral cavity 4; nasopharynx 2 and paranasal sinus 1. Stage (AJCC) II 13.6% pts, stage III 41% and stage IV 45%. Nuclear DNA content was measured by image analysis on paraffin-embedded samples. There were 9 diploid and 13 aneuploid tumors. Determination of cell-cycle kinetics was also performed on all tumors. Increased of percentage in S-G_2M phase was observed in 5 tumors.Response rate was 100% (95% complete response). The median follow-up was 23.5 months (range 12-39 m). The 18-month actuarial local control and overall survival were 45% and 77%, respectively. The local control was 55% and 43% in diploid and aneuploid tumors ($p > 0.05$) and there was not difference in survival.
Our findings suggest that DNA content has not a predictive value in HNC treated with HRT.

Leukaemia and Myeloma

819

FLUDARABINE A MAJOR NEW DRUG IN CHRONIC LYMPHOCYTIC LEUKEMIA (CLL)

MJ Keating, S O'Brien, LE Robertson, & H. Kantarjian
University of Texas M.D. Anderson Cancer Center, Houston, Texas 77030, USA

Fludarabine is a purine analog which has shown activity in lymphoid malignancy. Since 1984, four clinical trials have been conducted in prior treated patients (pts), fludarabine as a five-day regimen ± prednisone, a once a week schedule and a three day schedule. Of 374 pts, 120 (32%) obtained a CR and 61 (16%) a PR. Important prognostic factors included stage, age, hemoglobin, platelet levels, albumin, and β-2-microglobulin. The median survival was 18 months with no difference in survival between CR and PR pts. The five-day schedule had a higher response rate than the three-day schedule and the least encouraging results were noted with the once-a-week schedule. In addition, 155 untreated pts have received the five-day schedule ± prednisone. Ninety-nine (64%) achieved a CR and 23 (15%) a PR. 70% are projected to be alive five years after treatment with a significant effect of CR on survival. Age, stage, and lactic dehydrogenase level were important prognostic factors for response and survival. The major morbidity is fever and infection related to myelosuppression and immunosuppression. Opportunistic organisms were more common with fludarabine + prednisone. Multivariate analysis has been used to develop predictive models for response and survival in both previously untreated and previously treated pts. Fludarabine appears to be the most active single agent studied in CLL.

820

FLUDARABINE + ARA-C + G-CSF (FLAG) TREATMENT OF NEWLY-DIAGNOSED AML and MDS.

ESTEY E, Plunkett W, Gandhi V, Keating M, University of Texas M.D. Anderson Cancer center, Houston, USA

We have given 92 patients with newly-diagnosed AML (n=58) or MDS (n=34) a pharmacodynamically designed schedule of Fludarabine + ara-C (FA) with G-CSF 400 μg/m² given 1 day before, during and after chemotherapy (until CR). Results following FLAG were compared with those seen in 85 patients (54 AML, 31 MDS) given FA in an immediately preceding study. The 92 FLAG and the 85 FA patients were similar in terms of known proghostic variables (median age 60-65, 33-39% with abnormalities of chromosomes 5 and/or 7). The CR rate to date is 45/85 for FA vs 63/92 for FLAG ($p = .03$). With each regimen response rates were similar for AML and MDS patients. Days to >1000 neutrophils were on average 10 days shorter with FLAG than FA. Nonetheless 29 and 43 day survival rates were similar with the 2 regimens with patients not on CR at these times having persistent leukemia. This suggests that the improved CR rate with FLAG is due to sensitization of blasts to FA by G-CSF. In vitro and in vivo data to be presented demonstrates that G-CSF enhances active nucleotide accumulation providing a possible explanation for this sensitization.

821

COMPARISON OF 5 DAY (12 mg/m²) VERSUS SINGLE HIGH DOSE (100 mg/m²) MITOXANTRONE REGIMEN AS INDUCTION THERAPY FOR AML.

W.R. Bezwoda, R. Dansey, L. Dreosti, L. Seymour. Division of Hematology/Oncology, University of Witwatersrand, Johannesburg, South Africa.

Mitoxantrone has been shown to be an effective induction chemotherapy for AML but optimal schedules have not been established. In a pilot study 8/8 patients with de novo AML achieved CR following one single dose of mitoxantrone 100 mg/m² without major toxicity. Following this pilot investigation a randomised study comparing Mitoxantrone 12 mg/m² x 5 vs Mitoxantrone 100 mg/m² x 1 was undertaken. Of 21 patients entered, 7/11 achieved CR with the 5 day regimen and 10/10 achieved CR with the single high dose therapy. Toxicity from high dose mitoxantrone was no greater than that seen after other leukemic induction regimens. Stomatitis was mild in all cases and there was no cardiotoxicity Hematologic recovery occured on day 21-33. Patients in this ongoing study are being randomised to early autografting versus 6 cycles of conventional maintenance chemotherapy.

822

LONG-TERM RESULTS OF A REGIMEN FOR TREATMENT OF AML

Goldschmidt E, Machover D, Itzhaki M, and Misset JL
SMST - Hôpital Paul-Brousse, Villejuif - France

We updated the results of a regimen for treatment of AML previously published in part (Cancer 53:1644-50, 1984) which consisted of intensive induction chemotherapy (ADM, VCR, ARA-C), early consolidation with the same chemotherapy as for induction, splenectomy and long-term continuous maintenance chemotherapy for 5 years (y) with 6-MP and MTX together with periodic reinforcements with DNR and VCR. The study was performed between 1976 and 1983. Forty patients entered the trial. Of these, 35 attained a CR and 31 could be splenectomized. The characteristics of the 31 patients were : median age : 34 y (range 11-61) ; sex : 18 F, 13 M ; cell types : 14 myeloblastic, 7 promyelocytic, 10 myelomonocytic ; 17 had extra medullary bulky disease. The median follow-up time for the 31 patients is 7.5 y. The DFS is 48% ± 19% from 7.5 y to 17 y. The median duration of CR is 7.5 y. The characteristics that carried a bad prognosis upon DFS were age ≥ 40 y ($p=0.02$), and the myelomonocytic cell-type ($p=0.007$). Median survival is 7.5 y. The probability of being alive at 10 y is 45% ± 18% and at 13 y it is 40% ± 18%. The differences between long-term DFS and survival are explained because 3 patients in long-term CR died (two died suddenly of unknown cause and one had pneumococcal infection). Procreation was observed in 3 patients (2 F ; 1 M). From the result of this small series we believe it important to reconsider the components of this therapeutic strategy in further studies.